REMARKS/ARGUMENTS

The Pending Claims

Claims 29-49 are pending and are directed to a modified DnaK protein (claims 29-37), a composition comprising the modified DnaK protein (claims 38 and 39), a method of using the modified DnaK protein (claim 40), and a method of producing a modified DnaK protein (claims 41-49).

Amendments to the Specification

The specification has been amended to include a "Cross-Reference to Related Applications" section, to correct typographical errors, and to capitalize trademarked terms. No new matter has been added by way of these amendments to the specification.

Amendments to the Claims

Elected claims 8-16 have been rewritten as new claims 29-49. The new claims are supported by the originally filed claims, as well as in the specification at, for example, page 1, lines 10-13, page 22, lines 27-19, page 23, lines 1-9, and page 24, lines 17-23. Claims 1-28 have been canceled. Accordingly, no new matter has been added by way of these amendments to the claims.

Summary of the Office Action

The Office requests that Applicants amend the specification to contain a "Cross-Reference to Related Applications" section, correct typographical errors, and capitalize trademarked terms.

The Office objects to claims 8-13 for using the phrase "characterized by" and "composed of" instead of "comprising" or "consisting of."

The Office rejects claims 8-13 under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter.

The Office rejects claims 8-13 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite.

The Office rejects claims 8-13 under 35 U.S.C. § 112 as allegedly failing to comply with the written description requirement.

The Office rejects claims 8-13 under 35 U.S.C. § 102(a) as allegedly anticipated by Chesnokova et al., *Biochemistry*, 42: 9028-9040 (2003).

The Office rejects claims 8-10 under 35 U.S.C. § 102(b) as allegedly anticipated by Zhang et al., *Journal of Biological Chemistry*, 271: 19668-19674 (1996).

The Office rejects claims 8-12 under 35 U.S.C. § 102(b) as allegedly anticipated by Swain et al, *Biochemical Society Symposium*, 68: 69-82 (2001).

The Office rejects claims 8-10 and 13 under 35 U.S.C. § 102(b) as allegedly anticipated by Zhang et al., *Archives of Biochemistry and Biophysics*, 356: 177-186 (1998).

Reconsideration of these objections and rejections is hereby requested.

Discussion of the Objections to the Specification

The Office requests that Applicants update the application to include reference to PCT/JP04/09785, filed July 2, 2004, which claims the benefit of Japanese Patent Application No. 2003-191081, filed on July 3, 2003. Applicants note that the priority information is included in the application data sheet, which was filed with the application. However, Applicants also have amended the specification to include a "Cross-Reference to Related Applications" section in accordance with the Office's request.

Additionally, Applicants have amended the specification to correct typographical errors and to capitalize trademarked terms.

Accordingly, Applicants request that the objections to the specification be withdrawn.

Discussion of the Objections to the Claims and the Utility, Indefiniteness, and Written Description Rejections

The amendments to the claims are believed to render moot (i) the objections to the claims, (ii) the utility rejection, (iii) the indefiniteness rejection, and (iv) the written

description rejection. Accordingly, Applicants request that the respective objections and rejections be withdrawn.

Discussion of the Section 102(a) Rejection

The Office contends that Chesnokova et al. anticipates the claimed invention. Chesnokova et al. published online on July 12, 2003, which is less than one year before the earliest effective U.S. filing date for the present application (which is the July 2, 2004 filing date of International Patent Application PCT/JP04/09785). Applicants will provide evidence that the Japanese priority document (Japanese Patent Application No. 2003-191081, filed on July 3, 2003) supports the pending claims and evidences an invention date prior to the publication date of Chesnokova et al. Therefore, Chesnokova et al. is not prior art to the pending claims, and this anticipation rejection will be rendered moot.

Discussion of the Section 102(b) Rejections

The Office contends that each of Zhang et al. (1996), Swain et al., and Zhang et al. (1998) anticipate the claimed invention. These rejections are traversed for the following reasons.

A. Discussion of the Claimed Invention

The pending claims are directed to a method for producing a modified DnaK protein with improved blocking efficiency, as well as the modified DnaK protein produced by this method. The modified DnaK protein is produced by deleting the ATPase domain of a DnaK protein. Additionally, a hydrophobic inside of a β-sheet domain of the DnaK protein is exposed by deleting a part of the β-sheet domain and/or substituting at least one hydrophilic amino acid in the β-sheet domain with a hydrophobic amino acid.

The inventors discovered that when a protein consisting of a hydrophobic domain and a hydrophilic domain is used as a blocking agent against the hydrophobic surface, the hydrophobic domain of the protein is absorbed to the hydrophobic surface due to the hydrophobic interaction. This allows the hydrophobic surface to be covered with the hydrophilic domain of the protein, resulting in efficient blocking of the hydrophobic surface (see, e.g., Figure 3, and page 13, lines 3-8, of the specification).

Based on this finding, the inventors desired to produce a modified DnaK protein with further improved blocking efficiency using a DnaK protein from which the ATPase domain has been deleted. The DnaK protein includes (a) a hydrophobic domain (at positions 384-502) having a β-sheet structure and (b) a hydrophilic domain (at positions 509-607) having an α helix structure (see, e.g., Figure 4, and page 15, lines 1-9, of the specification).

The inventors hypothesized that a protein with improved blocking efficiency could be obtained by enhancing the hydrophobicity of the hydrophobic domain that interacts with the hydrophobic surface. Therefore, the inventors enhanced hydrophobicity by deleting the amino acid sequence from the N terminus (thereby breaking the hydrophobic domain) (see, Figure 8, and page 16, lines 17-19, of the specification).

In particular, in order to obtain a protein with improved blocking efficiency, the hyper-hydrophobic domain in the hydrophobic domain can be exposed by deleting the amino acid sequence from the N terminus through a portion of the β-sheet structure (see, e.g., Figure 9, and page 23, lines 23-34, of the specification). The deletion of a part of the β-sheet structure can be conducted by removing the β-sheet portion adjacent to a hinge portion of the horseshoe-shaped structure in the substrate binding domain (see, e.g., page 24, lines 17-23, of the specification).

The spatial relationship of the domains of the DnaK protein is further elucidated by Figures A and B submitted herewith. Figure A demonstrates the spatial configuration of a fragment consisting of the amino acids at positions 389-607 of the DnaK protein (see also http://www.rcsb.org/pdb/explore.do?structureId=1DKX). In particular, Figure A illustrates the spacial relationship of the hydrophilic domain, hydrophobic domain, hyper-hydrophobic domain, and β-sheet structure. Figure B illustrates the relationship between the spatial configuration of the fragment and the amino acid positions of the DnaK protein. In addition, Figure C, which also is submitted herewith, illustrates that a modified DnaK protein from which the ATPase domain and a part of the β-sheet domain are deleted (i.e., a modified DnaK protein of amino acids 419-618) is more intensely absorbed to the hydrophobic surface via the exposed hyper-hydrophobic domain than a DnaK protein from which only the ATPase domain is deleted (i.e., a modified Dnak protein of amino acids 384-638). Thus, the modified

DnaK protein of amino acids 419-638 has improved blocking efficiency as compared to DnaK protein of amino acids 384-638.

Additionally, the inventors discovered that hydrophobicity of the hydrophobic domain could be enhanced by substituting one or more hydrophilic amino acids in the hydrophobic domain with a hydrophobic amino acid (see Figure 9).

B. Distinguishing the Claimed Invention over the Prior Art

Zhang et al. (1996) discloses a fragment that consists of amino acids 506-543 of the DnaK protein. As shown in Figure A submitted herewith and Figure 6 of the specification, the β-sheet of the DnaK protein is not contained in amino acids 506-543. Since the fragment disclosed in Zhang et al. (1996) lacks all of the amino acids of the β-sheet, the fragment differs from that of the pending claims, which recite that only a part of the β-sheet is deleted such that the remaining portion of the β-sheet is still present in the claimed protein.

Swain et al. discloses a fragment that consists of amino acids 387-552 of the DnaK protein. As shown in Figure A submitted herewith, the fragment disclosed in Swain et al. contains the entire β-sheet. This differs from the pending claims, which recite that a part of the β-sheet is deleted.

Zhang et al. (1998) discloses fragments that separately consist of (i) amino acids 384-638, (ii) amino acids 386-561, (iii) amino acids 389-607, and (iv) amino acids 607-638 of the DnaK protein. Of these, fragments (i), (ii), and (iii) include the entire β-sheet of the DnaK protein. This differs from the pending claims, which recite that a part of the β-sheet is deleted.

Fragment (iv) of Zhang et al. (1998) lacks the entire β-sheet of the DnaK protein. This differs from the pending claims, which recite that only a part of the β-sheet is deleted such that the remaining portion of the β-sheet is still present in the claimed protein.

Moreover, Zhang et al. (1996), Swain et al., and Zhang et al. (1998) do not teach substituting at least one hydrophilic amino acid in the β-sheet domain with at least one hydrophobic amino acid, as recited by the pending claims.

For these reasons, the pending claims are not anticipated by the cited references, and the anticipation rejections should be withdrawn.

Furthermore, none of the cited references provides any suggestion to modify a DnaK protein in such a way as to arrive at the modified DnaK protein of the invention (i.e., by deleting an ATPase domain and exposing a part of a hydrophobic inside of a β-sheet domain by (i) deleting a part of the β-sheet domain and/or (ii) substituting at least one hydrophilic amino acid in the β-sheet domain with a hydrophobic amino acid). Indeed, one of ordinary skill in the art would not have reasonably predicted that a DnaK protein modified in accordance with the present invention could have a higher blocking efficiency than the non-modified DnaK protein. Thus, the subject matter of the pending claims cannot be considered to be obvious in view of the cited references, whether considered alone or in combination.

Conclusion

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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